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ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/590,686	RAUCH ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-42,44-46 and 48-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-42,44-46 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/8/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 28-42, 44-46 and 48-50 are pending and examined on merits in this office action to the extent they encompasses the elected species.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 28-42, 44-46 and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Although specific claims may be discussed in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occurs.

5. Claim 28 recites “heterophilic antibodies” in line 3. The term “heterophilic antibodies” is not clearly defined in the specification although the words “human anti-mouse antibody” is placed in parentheses after the term “heterophilic antibodies” in line 9 on page 4 of the specification. It is unclear what do the words in the parentheses indicate? That is, it is unclear as to whether Applicants intended to define heterophilic antibodies by “human anti-mouse antibody” or is intended to show an example of a heterophilic antibody. Further, it is unclear what type of antibody Applicants are intended to include in the claim by the term “heterophilic antibodies”. There is no commonly accepted definition for the term “heterophilic antibody” (see the attached reference of Kaplan *et al*, 1999). Contrary to the instant specification, the attached reference defines heterophilic antibodies as weak antibodies with

multispecific activities against poorly defined antigens and excludes "human anti-animal antibodies" that develop as a result of treatments with animal immunoglobulins from the definition as the antibody shows strong avidities and are produced against well defined antigens. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See In re Hill, 161 F.2d 367, 73 USPQ 482 (CCPA 1947).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 28, 32, 34-38, 42 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated Figard (US 5,616,460).

With regard to claim 28, Figard discloses aqueous composition suitable for use as a buffer in immunoassay method involving binding of specific binding pairs (e.g. antibody-antigen binding) and the composition comprises a biological buffer to control pH and ethylene glycol (i.e. compound A) (Abstract; column 2, lines 40-67 and column 3, lines 31-32). Figard teaches that the composition can also include at least one biological detergent, at least one source of positive and negative counterions, e.g. salt, and at least one viscosity modifier, e.g. sugar (column 2, lines 44-47 and column 5, lines 1-5). Figard teaches that the composition comprising non-ionic detergents reduces non-specific binding of antibodies other than the analyte

antibodies (column 5, lines 6-35). Figard teaches that the antibodies other than the analyte antibodies (i.e. heterophilic antibodies) may adhere to the solid phase in the immunoassay for reason other than the specific recognition of their complementary antigen and this non-specific binding leads to false positive result (column 5, lines 6-15) and therefore, Figard teaches that the sample contains non-specific antibodies (i.e. heterophilic antibodies).

With regard to claim 32, as described above, the reaction mixture may comprise suitable source of positive and negative counterions (column 2, lines 44-47), as for example NaCl (column 5, lines 65-68).

With regard to claims 34 and 35, as described above, the reaction mixture comprises biological buffer and ethylene glycol, and the biological buffer includes MES, HEPES and PIPES (column 3, line 30 to column 4, line 19).

With regard to claim 36, Figard discloses 4-5% ethylene glycol (Column 6, lines 25-34), which is within the range of 0.5 to 25% and thus the claim is anticipated.

With regard to claims 37 and 38, Figard teaches Tween 20 as biological detergent and Tween 20 reads on the compound of claim 37 (column 5, line 20).

With regard to claim 42, Figard discloses preferred pH of the composition is 6.6 (column 2, line 52) and the pH reads on the adjusted pH value of 5.6-9.6.

With regard to claim 43, as described above, the composition is capable of reducing unspecific binding reaction of the binding pair (column 5, lines 6-15 and 36-38).

With regard to claim 47, the composition being capable of unspecific binding reaction would inherently increase the binding activity of affinity of antibodies.

With regard to claim 48, Figard teaches antibody antigen binding pair (column 1, lines 6-9).

With regard to claim 50, a sample suspected of containing human anti-mouse antibody does not positively indicate that the sample in fact contains the antibody and since the buffer composition being the same as that of instant application, it would be able to detect the analyte by the process as described above.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 28, 32, 33 34-40, 41-42, 48-49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salomen (GB 2062224A).

Salomen discloses an immunoassay method wherein the immunoassay method comprises reaction of the binding pair member in a solution comprising phosphate buffer, polyethylene glycol (i.e. compound A), a non-ionic detergent (e.g. Tween 20), and NaCl (See Examples 1 and 3). Serum samples and antibodies against the analyte are diluted in this buffer. The composition in the reaction mixture being

comprising the same reaction components would inherently reduce unspecific binding reaction of the binding pair.

Salome does not mention that the sample for detection of analyte is known or suspected of containing heterophilic antibodies.

However, the term "suspected of containing heterophilic antibody" does not positively indicate that the sample contains heterophilic antibodies and therefore, the immunoassay method of Salomen would be capable of detecting an analyte in the sample suspected of containing a heterophilic antibodies. Further, as defined in the attached reference (see the attached reference of Kaplan *et al*, 1999), heterophilic antibodies are weak antibodies with multispecific activities against poorly defined antigens and thus the reaction mixture being comprising the same reaction components would inherently reduce non-specific interference of the heterophilic antibodies.

With regard to claim 32, as described above, the reaction mixture comprises NaCl.

With regard to claims 34 and 35, as described above, the reaction mixture comprises phosphate buffer and polyethylene glycol.

With regard to claim 36, Salomen discloses 4% and 3% polyethylene glycol (See Examples 1 and 3), which falls within the range of 0.5 to 25% and thus the claim is anticipated.

With regard to claim 37, Salomen teaches Tween 20 in the reaction mixture and Tween 20 reads on the compound of claim 37.

With regard to claim 38, as described above, Salomen teaches Tween 20.

With regard to claim 39, Salomen teaches 0.1% Tween 20, which anticipates claim 39 as the value (0.1%) falls within the range of 0.1 to 1.0%.

With regard to claim 41, the reaction mixture of Salomen does not contain dithiothretol.

With regard to claim 42, Salomen discloses that the pH of phosphate buffer is 7.2 and the pH reads on the adjusted pH value of 5.6-9.6.

With regard to claim 43, as described above, the composition in the reaction mixture being comprising the same reaction components would inherently have the capability of reducing unspecific binding reaction of the binding pair.

With regard to claim 47, the composition being capable of unspecific binding reaction would inherently increase the binding activity of affinity of antibodies.

With regard to claim 48, Salomen teaches antibody antigen binding pair.

With regard to claims 33, 40 and 49 Salomen discloses different concentration of the components in the reaction buffer composition but however, does not disclose ratio of non-ionic detergent to polyethylene glycol, ionic strength. However, salomen discloses 3% PEG and) 1% Tween, i.e. a ratio of 1:30 (see example 3). However, the adjustment of particular working conditions (such as ionic strength, ration of different reaction components) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and therefore obvious under 35 U.S.C. § 103(a).

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence

indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 49, the substitution of the antibody-antigen binding pair with other binding pair such as receptor-ligand binding pair, as claimed, is considered to be an obvious variation for detection of different analyte, i.e. one of ordinary skill in the art would expect such a substitution of one binding pair with another to result in an equivalently useful immunoassay for detection of different analytes

With regard to claim 50, as described above, a sample suspected of containing human anti-mouse antibody does not positively indicate that the sample in fact contains the antibody and since the buffer composition being the same as that of instant application, it would be able to detect the analyte by the process as described above.

10. Claims 33, 39, 40, 44-46 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Figard (US 5,616,460).

See the above teaching of Figard for composition of an aqueous solution for an immunoassay. Figard discloses different concentration of the components in the

reaction buffer composition, but however, does not mention ratio of non-ionic detergent to ethylene glycol and ionic strength of the aqueous solution.

However, the adjustment of particular working conditions (such as ionic strength, ration of different reaction components) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and therefore obvious under 35 U.S.C. § 103(a) absent unexpected results.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 49, the substitution of the antibody-antigen binding pair with other binding pair such as receptor-ligand binding pair, as claimed, is considered to be an obvious variation for detection of different analyte, i.e. one of ordinary skill in the art would expect such a substitution of one binding pair with another to result in an equivalently useful immunoassay for detection of different analytes.

11. Claims 28, 29, 30-33, 34-40, 41-42, 44-46, 48-49 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Siedel *et al* (US 4,485,177).

With regard to claim 28, Siedel teaches a reagent suitable for use in an immunoassay method involving binding of specific binding pairs (e.g. antibody-antigen binding) and the reagent comprises a buffer to control pH (e.g. phosphate buffer), Tween 20 non-ionic detergent and a salt (e.g. NaCl) (see example 2, lines 25-47 of column 10). The reagent preferably also contains a substance wherein the substance is polyethylene glycol (column 6, lines 41-49). The composition in the reaction mixture being comprising the same reaction components would inherently reduce unspecific binding reaction of the binding pair.

Siedel does not mention that the sample for detection of analyte is known or suspected of containing heterophilic antibodies.

However, the term "suspected of containing heterophilic antibody" does not positively indicate that the sample contains heterophilic antibodies and therefore, the immunoassay method of Salomen would be capable of detecting an analyte in a sample suspected of containing a heterophilic antibodies. Further, as defined in the attached reference (see the attached reference of Kaplan *et al*, 1999), heterophilic antibodies are weak antibodies with multispecific activities against poorly defined antigens and thus the reaction mixture being comprising the same reaction components would inherently reduce non-specific interference of the heterophilic antibodies.

With regard to claims 29 and 30, Siedel teaches that turbidimetric immunoassay further comprising BSA (column 6, lines 53-61).

With regard to claim 32 Siedel discloses the reaction mixture comprising NaCl (column 10, line 35).).

With regard to claims 34 and 35, as described above, the reaction mixture comprises phosphate buffer (column 10, line 25-46).

With regard to claim 36, Siedel discloses 0.1-8% polyethylene glycol (Column 6, lines 59-60), which has substantial overlapping with the concentration range of compound A of claim 36 and thus the claim is anticipated.

With regard to claims 37 and 38, Siedel teaches Tween 20 and Tween 20 reads on the compound of claim 37 (column 5, line 20).

With regard to claim 41, the reaction mixture of Siedel does not contain dithiothretol.

With regard to claim 42, Siedel discloses pH 7.2 of the composition (column 10, line 33) and the pH anticipates the adjusted pH value of 5.6-9.6.

With regard to claim 43, as described above, The composition in the reaction mixture being comprising the same reaction components would inherently reduce unspecific binding reaction of the binding pair.

With regard to claim 47, the composition being capable of unspecific binding reaction would inherently increase the binding activity of affinity of antibodies.

With regard to claim 48, Siedel teaches antibody antigen binding pair (column 2, lines 41-46 and Abstract).

With regard to claims 31, 33, 39, 40, 44-46 and 49 Siedel discloses different concentration of the components in the reaction buffer composition, but however, does not mention ratio of non-ionic detergent to ethylene glycol and the range of ionic strength of the aqueous solution. Siedel teaches different concentrations of buffer, PEG, albumin and a range of ionic strength of the buffer (column 6, lines 37-61 and column 7, lines 1-5). However, the adjustment of particular working conditions (such as ionic strength, ratio of different reaction components) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and therefore obvious under 35 U.S.C. § 103(a) absent unexpected results.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 49, the substitution of antibody-antigen binding pair with other binding pair such as receptor-ligand binding pair, as claimed, is considered to be an obvious variation for detection of different analyte, i.e. one of ordinary skill in

the art would expect such a substitution of one binding pair with another to result in an equivalently useful immunoassay for detection of different analytes.

With regard to claim 50, as described above, a sample suspected of containing human anti-mouse antibody does not positively indicate that the sample in fact contains the antibody and since the buffer composition being the same as that of instant application, it would be able to detect the analyte by the process as described above.

12. Claims 28-40, 41-42, 44-46, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stewart (US 6,503,702 B1).

With regard to claim 28, Stewart teaches immunoassay buffer system comprising a buffer to control pH (e.g. sodium carbonate, sodium borate or Tris-saline), a detergent, a salt, a stabilizing agent and a protein which is not recognized by any of the antibodies used in the assay (column 5, lines 48-55). The stabilizing agent can be polyethylene glycol, glycerol or ethylene glycol (column 6, lines 54-57), which reads on compound A of instant claim 28. The composition in the reaction mixture being comprising the same reaction components would inherently reduce unspecific binding reaction of the binding pair.

Stewart does not mention that the sample for detection of analyte is known or suspected of containing heterophilic antibodies.

However, the term "suspected of containing heterophilic antibody" does not positively indicate that the sample contains heterophilic antibodies and therefore, the immunoassay method of Salomen would be capable of detecting an analyte in a

sample suspected of containing a heterophilic antibodies. Further, as defined in the attached reference (see the attached reference of Kaplan *et al*, 1999), heterophilic antibodies are weak antibodies with multispecific activities against poorly defined antigens and thus the reaction mixture being comprising the same reaction components would inherently reduce non-specific interference of the heterophilic antibodies.

Therefore, the reference is deemed to anticipate independent claim 28.

With regard to claims 29, 30 and 31, Stewart teaches that the protein which is not recognized by any of the antibodies may be selected from BSA, ovalbumin, casein and fetal bovine serum at a concentration range of 0.1-2% (column 7, lines 25-40).

With regard to claims 32 and 33 Stewart teaches that the salt may be selected from NaCl and potassium chloride and the concentration of 140mM, which anticipates 100mM to 1.5M of claim 33 of instant application (column 6, lines 23-31).

With regard to claims 34, Stewart teaches the buffer can be Tris-saline buffer (column 5, lines 64-65), which reads on Tris (Tris(hydroxymethyl)-aminomethane buffer of instant claim 34.

With regard to claims 35, Stewart teaches that the stabilizing agent can be polyethylene glycol, glycerol or ethylene glycol (column 6, lines 54-57).

With regard to claim 36, Stewart teaches polyethylene glycol at 1% (column 6, line 59-60), which is within the concentration range of compound A of claim 36 and thus the claim is anticipated.

With regard to claims 37 and 38, Stewart teaches that the detergent can be Tween 20 and Tween 20 reads on the compound of claims 37 and 38 (column 6, line 17).

With regard to claim 41, the reaction system of Stewart does not contain dithiothretol.

With regard to claim 42, Stewart discloses pH between 7.5-8.5 of the buffer system (column 5, line 61) which lie within the range of 5.6-9.6 of instant claim 42 and thus the pH of the buffer system of Stewart anticipates the adjusted pH value of claim 42.

With regard to claim 43, as described above, the composition in the reaction mixture being comprising the same reaction components would inherently reduce unspecific binding reaction of the binding pair.

With regard to claim 47, the composition being capable of unspecific binding reaction would inherently increase the binding activity of affinity of antibodies.

With regard to claim 48, Stewart teaches antibody antigen binding pair (column 3, lines 35-63 and column 4, lines 24-37).

With regard to claims 39-40, 44-46 and 49 Stewart discloses different concentration of the components in buffer system, but however, does not mention ratio of non-ionic detergent to ethylene glycol and does not disclose the range of concentration of non-ionic detergent as claimed.

Siedel teaches different concentrations of buffer, stabilizing agent, salts, detergents and non-specific proteins (column 5, line 48 to column 7, line 40).

Stewart teaches different concentrations of non-ionic detergent and teaches that the concentration must be carefully chosen so that the dissolution of cellular material is balanced against the denaturing effects of the detergent (column 6, lines 6-11). The composition of the buffer system also being comprising the same composition of instant claim 28, would be capable of preventing low affinity binding and one of ordinary skill in the art can easily optimize different concentrations of the components of the buffer system to find an optimum K_D value for low-affinity binding with the expectation of increasing detection sensitivity, with a reasonable expectation of success. Further, the adjustment of particular working conditions (such as ionic strength, ratio of different reaction components) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and therefore obvious under 35 U.S.C. § 103(a) absent unexpected results.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

With regard to claim 49, the substitution of antibody-antigen binding pair with other binding pair such as receptor-ligand binding pair, as claimed, is considered to be an obvious variation for detection of different analyte, i.e. one of ordinary skill in the art would expect such a substitution of one binding pair with another to result in an equivalently useful immunoassay for detection of different analytes.

With regard to claim 50, as described above, a sample suspected of containing human anti-mouse antibody does not positively indicate that the sample in fact contains the antibody and since the buffer composition being the same as that of instant application, it would be able to detect the analyte by the process as described above.

Response to argument

13. Applicant's arguments and amendments filed 12/8/09 have been fully considered, and are persuasive to overcome the rejection of 9/15/09 under 35 USC 112 second paragraph and the rejections under 35 USC 102, but are not persuasive to overcome the rejections under 35 USC 102 (b) and 103(a) over Figard *et al*. Moreover, Applicants arguments necessitated new grounds of rejection under 35 USC 112 second paragraph and 35 USC 103 (a) as described in this office action.

With regard to Figard, Applicants argued that Figard does not disclose a method of reducing an influence of heterophilic antibodies present in a sample on the specific binding reaction of a binding pair.

The above argument is not persuasive because Figard discloses aqueous composition suitable for use as a buffer in immunoassay method involving binding of

specific binding pairs (e.g. antibody-antigen binding) and the composition comprises a biological buffer to control pH and ethylene glycol (i.e. compound A) (Abstract; column 2, lines 40-67 and column 3, lines 31-32). Figard teaches that the composition can also include at least one biological detergent, at least one source of positive and negative counterions, e.g. salt, and at least one viscosity modifier, e.g. sugar (column 2, lines 44-47 and column 5, lines 1-5). Figard teaches that the composition comprising non-ionic detergents **reduces non-specific binding of antibodies other than the analyte antibodies** (column 5, lines 6-35). Figard further teaches that the antibodies other than the analyte antibodies (i.e. heterophilic antibodies) may adhere to the solid phase in the immunoassay for reason other than the specific recognition of their complementary antigen and this non-specific binding leads to false positive result (column 5, lines 6-15). Therefore, Figard clearly teaches detection of analyte in a sample comprising non-specific antibodies (i.e. heterophilic antibodies) using the buffer composition as described above.

With regard to Salomen, Siedel and Stewart, Applicants argued that the references does not disclose a method of reducing an influence of heterophilic antibodies present in a sample on the specific binding reaction of a binding pair.

The above argument is not persuasive because the term "suspected of containing heterophilic antibody" does not positively indicate that the sample contains heterophilic antibodies and therefore, the immunoassay method of Salomen, Siedel and Stewart, would be capable of detecting an analyte in a sample suspected of containing a heterophilic antibodies. Further, as defined in the attached

reference of Kaplan (see the attached reference of Kaplan *et al*, Clinical Chemistry 1999), heterophilic antibodies are weak antibodies with multispecific activities against poorly defined antigens and thus the reaction mixture being comprising the same reaction components would inherently reduce non-specific interference of the heterophilic antibodies.

With regard to the declaration filed 12/8/09, the declaration has been fully considered but is not persuasive to overcome the rejections. The declaration demonstrated measurement of HAMA (i.e. human anti-mouse antibodies, more specifically, human immunoglobulins with specificity for mouse immunoglobulins) in the presence and absence of the buffer composition (i.e. Applicants' buffer composition: sample buffer) and demonstrated that less HAMA is detected in the presence of Applicants' buffer (sample buffer). Applicants have not clearly described what is meant by "HAMA effect" and how this "HAMA effect" is is related to reduction of specific binding of HAMA to mouse antibody in the detection of two binding partners (e.g. mouse antibody and its corresponding analyte) in the presence of HAMA. Applicants have not shown increased detection sensitivity of an analyte (i.e. detection of one binding partner with another corresponding binding partner) in a sample comprising HAMA in the presence of Applicants' buffer. Applicants' argued that based on prior art of record, one of ordinary skill in the art would have had no way of knowing that the influence of heterophilic antibodies on the specific binding reaction of a binding pair could be reduced by the presently claimed method (see Applicants remark on page 9 filed 12/8/09). However, the reference of Figard clearly

teaches reduction of the influence of heterophilic antibody (sample containing non-specific antibodies) on the specific binding of binding partners because Figard teaches that the antibodies other than the analyte antibodies (i.e. heterophilic antibodies) influences immunoassay for reason other than the specific recognition of their complementary antigen and this non-specific binding leads to false positive result (column 5, lines 6-15) and therefore, Figard clearly teaches that the composition comprising non-ionic detergents reduces the influence of antibodies other than the analyte antibodies (i.e. heterophilic antibodies) in the detection of specific binding of binding partners. Further, As described above in 35 USC 112 rejection, the term "heterophilic antibody" as described in the attached reference of Kaplan *et al*, are weak antibodies with multispecific activities against poorly defined antigens and excludes "human anti-animal antibodies" that develop as a result of treatments with animal immunoglobulins from the definition as the antibody shows strong avidities and are produced against well defined antigens. However, the affidavit is directed to HAMA, which from the attached reference, does not fall within the definition of heterophilic antibodies wherein Claim 28 is directed to heterophilic antibodies i.e. the antibodies as described by Figard and Kaplan.

Conclusion

14. Applicants' amendment necessitated new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicant should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (e.g., if the amendment is not supported in ipsis verbis, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Primary Examiner, Art Unit 1641